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EXAMINER	
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ART UNIT	PAPER NUMBER
1795	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

Office Action Summary	Application No.	Applicant(s)	
	10/595,771	SCHNELLE ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05/10/2006 (preliminary amndt.)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,36,38-42,44-49,52-63,65,66 and 68* is/are rejected.

7)☒ Claim(s) *37,43,50,51,64 and 67* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/09/2006*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 35, 39-42, 45, 52, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Müller et al. US 6,492,175 B1 ("Müller").

Addressing claim 35, Müller discloses a method for analyzing at least one deformable object in a suspension fluid (abstract), comprising the steps of:

generation of an electric positioning field and positioning of the object in positioning field (col. 02:66 – col. 03:15; col. 04:58 – col. 05:14; col. 09:25-39; and col. 05:29-40);

generation of an electric deformation field (electroporation) so as to exert a deformation force on the object (col. 05:21-37; col. 02:66 – col. 03:14; col. 09:25-39; and col. 08:54 – col. 09:05); and

detection of at least one property selected from the group consisting of dielectric, geometric and optical properties of the object (col. 09:49-59) ,

wherein the positioning field is generated in a compartment of a fluidic microsystem (abstract and col. 03:24-32), and the positioning of the object takes place in a contactless manner without electrode contact or in a freely suspended state

(col. 05:04-14; col. 05:29-37; col. 03:33-39; col. 02:49-59; and Figures 1-3).

Addressing claim 39, for the additional limitation of this claim see Figures 1-3 and col. 04:37-45.

Addressing claims 40 and 41, for the additional limitations of these claims see Figures 1-3; col. 04:37-45; col. 06:54 – col. 07:10; and col. 09:53-58. The field cage may be open or closed. See also col. 05:29-49.

Addressing claim 42, for the additional limitation of this claim see col. 05:29-49.

Addressing claim 45, for the additional limitation of this claim see col. 08:54-58.

Addressing claim 52, for the additional limitation of this claim see Figure 7 and col. 07:47-65. Note cells 74 lined-up for selection for deformation.

Addressing claim 53, for the additional limitation of this claim see col. 01:01-11.

3. Claims 59-61 and 63 are rejected under 35 U.S.C. 102(b) as being anticipated by Chang US 4,970,154 ("Chang").

Addressing claim 59, Chang discloses a measuring apparatus for analyzing at least one object (abstract), said measuring apparatus comprising:

a fluidic microsystem having a compartment containing at least one electrode arrangement (microtitre culture plate – col. 12:46-65);

a detector device adapted to measure electric, geometric and/or optical properties of the object (see col. 16:01-22, which discloses freeze-fracture electron microscopy; col. 16:25-41, which discloses fluorescent imaging; and col. 13:19-40, which discloses measuring the actual electrical field applied to the objects); and

a field forming device comprising at least one high-frequency generator

(Figure 14, col. 11:21-25; col. 13:08-22; and col. 10:50-59), wherein the field forming device can be switched between an operating state in which a high-frequency

positioning field is generated in the compartment by the at least one electrode arrangement and an operating state in which a deformation field is generated in an analysis area by the at least one electrode arrangement (Figure 14, col. 11:21-25; col. 13:08-19; and col. 10:50-59).

Addressing claim 60, for the additional limitation of this claim see col. 13:08-19.

Addressing claim 61, for the additional limitation of this claim see col. 16:01-22, which discloses freeze-fracture electron microscopy. Also see Figures 18A-C.

Addressing claim 63, for the additional limitation of this claim notice the triggering circuit in Figure 14. Also see col. 13:19-40.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 35, 36, 38, 44-49, 53-59, 62, 65, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang US 4,970,154 ("Chang") in view of WO 03/035264 A1 as evidenced by US 2005/0040044 A1 ("Frenea"). Note that except for the abstract WO 03/035264 A1 is in French. However, since US 2005/0040044 A1 is written in English and is the national stage "371" of WO 03/035264 A1 it is *prima facie* an accurate English language translation of WO 03/035264 A1. See 35 U.S.C. 371

(c)(2) and MPEP 1893.01(d). As such, although the rejection is based on WO 03/035264 A1, as a secondary reference, all citations will be from US 2005/0040044 A1 instead.

Addressing claim 35, Chang discloses a method for analyzing at least one deformable object in a suspension fluid (abstract), comprising the steps of:

generation of an electric positioning field and positioning of the object in positioning field (abstract – "The alternating electrical field induces cell congregation by the process of dielectrophoresis." Also, see col. 03:63-68; col. 10:43-54; col. 11:21-25; and col. 06:25-30);

generation of an electric deformation field (electroporation or electrofusion in Chang) so as to exert a deformation force on the object (abstract – "The high-power pulsed radiofrequency electrical field prorates or fuses the cells." Also see col. 03:50-62; col. 04:16-31; and col. 06:30-35); and

detection of at least one property selected from the group consisting of dielectric, geometric and optical properties of the object (col. 04:44-47; col. 06:25-35; Chang col. 13:35-40, which discloses measuring and recording the actual electrical field as it is applied to the cells; .and col. 11:10-13) ,

wherein the positioning field is generated in a compartment of a fluidic microsystem (Figure 4a and col. 11:10-17. Note the spacers 37 of approximately 0.3

mm thickness), and the positioning of the object takes place in a contactless manner without electrode contact or in a freely suspended state (note that the electrodes 25 are outside the compartment (Figures 4a and 4b)).

Chang does not mention whether the object is positioned in a potential minimum of the positioning field, although the electric positioning field is a dielectrophroresis field (abstract – "The alternating electrical field induces cell congregation by the process of dielectrophoresis." Also, see col. 03:63-68; col. 10:43-54; col. 11:21-25; and col. 06:25-30).

Frenea discloses a system of handling dielectric particles, particularly biological cells, by means of dielectrophoresis. The system of Frenea generates an electric positioning field to position an object in a potential minimum of the positioning field and also generates an electric deformation field (such as electroposition field) so as to exert a deformation force on the object. See the title, abstract, specification paragraph [0003] (bracketed numbers will refer to specification paragraph unless otherwise indicated), and [0033]. It would have been obvious to one with ordinary skill in the art at the time of the invention to substitute the electrode system of Frenea for that in the Figure 4 embodiment of Chang because (1) as taught by Frenea it provides a high density or high degree of integration so that a large number of objects may be manipulated ([0004], [0009], and [0024]), and (2) it is structurally and electrically compatible with the electrode system in Chang. In regard to the latter point, Frenea discloses that the electrodes may be formed on a plate of glass ([0023]) and Chang discloses that glass plates may be used to from the compartment walls (col. 11:10-18) and that the

electrodes may in wide variety of forms including interdigitated arrays (col. 04:48-54). Also, Chang already has a power source for generating a dielectrophoresis field, which can generate very complicated wave forms (col. 13:19-40).

Addressing claim 36, arguably claim 36 is already met by Chang since Chang uses dielectrophoresis to position the object and the dielectrophoresis must be either negative dielectrophoresis or positive dielectrophoresis. In any event, Frenea discloses using negative dielectrophoresis to position the object. See the abstract and [0005].

Addressing claim 38, for the additional limitation of this claim see in Chang col. 04:44-47; col. 11:10-13; and col. 06:25-35.

Addressing claim 44, for the additional limitation of this claim see in Chang col. 10:01-30, especially col. 10:28-30.

Addressing claim 45, for the additional limitation of this claim see in Chang col. 10:01-30

Addressing claim 46, for the additional limitation of this claim see in Chang col. 13:40-59.

Addressing claim 47, for the additional limitation of this claim see in Chang col. 17:05-20, which discloses monitoring the effect a deformation field after several generations of the deformation field. To do so in an alternating manner a number of times one after the other is an obvious variant, the frequency of the monitoring just depends on the desired extent of detail of the deformation process.

Addressing claim 48, for the additional limitation of this claim see in Chang col. 17:05-20, note "4 minutes".

Addressing claim 49, for the additional limitation of this claim see in Chang col. 08:16-21, which discloses varying the pulsed radiofrequency "to achieve the proper resonant frequency for the cells of interest." Thus, claim 49, in light of Chang, is jus optimization of the deformation field as the deformation is occurring.

Addressing claim 53, for the additional limitation of this claim see in Chang col. 01:01-20 and Frenea [0001].

Addressing claim 54, although Chang as modified by Frenea does not specifically mention making a distinction between normal and altered cells or between normal cells having different physiological properties as a function of the detected dielectric, geometric, and/or optical properties it would have been obvious to do so

because Chang discloses, for example, altering cells for gene therapy by introducing the altered cells into a patient. See col. 03:03-24. So, clearly it is important for the health of the patient to distinguish between cells that have been alerted as desired from those not so altered before they are introduced into the patient. Note also col. 16:01-22, which discloses freeze-fracture electron microscopy, and col. 16:25-41, which discloses fluorescent imaging.

Addressing claim 55, although Chang as modified by Frenea does not specifically stem cells clearly a wide variety of cells are contemplated, particularly medically significant cells. See col. 01:01-40; col. 03:01-24; and col. 04:16-31. So to use the method with stem cells, barring a contrary showing, such as unexpected or results, is just a use of particular cells that are recently gaining medical significance that would not require any special modification of the method.

Addressing claim 56, for the additional limitation of this claim note Chang col. 13:35-40, which discloses measuring and recording the actual electrical field as it is applied to the cells. So, detecting at least parameters such as frequency of the positioning field, frequency of the deformation field, voltage of the positioning field, and voltage of the deformation field as disclosed. Chang also discloses optically monitoring poration or fusion, so also at least duration of the individual deformations and duration of a number of deformations is also disclosed. See col. 04:44-47 and col. 17:05-20. Note also col. 16:01-22, which discloses freeze-fracture electron microscopy, and

col. 16:25-41, which discloses fluorescent imaging.

Addressing claims 57 and 58, for the additional limitation of this claim note Chang col. 13:35-40, which discloses measuring and recording the actual electrical field as it is applied to the cells during cell fusion. Chang also discloses optically monitoring poration or fusion, so also at least duration of the individual deformations and duration of a number of deformations is also disclosed. See col. 04:44-47 and col. 17:05-20. Since cell fusion is the formation of cell pairs or cell aggregates claims 57 and 58 are, if not implied, then obvious. Note also col. 16:01-22, which discloses freeze-fracture electron microscopy, and col. 16:25-41, which discloses fluorescent imaging.

Addressing claim 59, Chang discloses a measuring apparatus for analyzing at least one object (abstract), said measuring apparatus comprising:

a fluidic microsystem having a compartment in contact with at least one electrode arrangement (Figure 4a and col. 11:10-17. Note the spacers 37 of approximately 0.3 mm thickness);

a detector device adapted to measure electric, geometric and/or optical properties of the object (see col. 16:01-22, which discloses freeze-fracture electron

microscopy; col. 16:25-41, which discloses fluorescent imaging; and col. 13:19-40, which discloses measuring the actual electrical field applied to the objects); and

a field forming device comprising at least one high-frequency generator (Figure 14, col. 11:21-25; col. 13:08-22; and col. 10:50-59), wherein the field forming device can be switched between an operating state in which a high-frequency positioning field is generated in the compartment by the at least one electrode arrangement and an operating state in which a deformation field is generated in an analysis area by the at least one electrode arrangement (Figure 14, col. 11:21-25; col. 13:08-19; and col. 10:50-59).

In the Figure 4 embodiment of Chang although the electrode arrangement is in contact with the compartment it is not contained by the compartment.

Frenea discloses a system of handling dielectric particles, particularly biological cells, by means of dielectrophoresis. The system of Frenea generates an electric positioning field to position an object in a potential minimum of the positioning field and also generates an electric deformation field (such as electroposition field) so as to exert a deformation force on the object. See the title, abstract, specification paragraph [0003] (bracketed numbers will refer to specification paragraph unless otherwise indicated), and [0033]. It would have been obvious to one with ordinary skill in the art at the time of the invention to substitute the electrode system of Frenea for that in the Figure 4 embodiment of Chang because (1) as taught by Frenea it provides a high density or high degree of integration so that a large number of objects may be manipulated

([0004], [0009], and [0024]), and (2) it is structurally and electrically compatible with the electrode system in Chang. In regard to the latter point, Frenea discloses that the electrodes may be formed on a plate of glass ([0023]) and Chang discloses that glass plates may be used to from the compartment walls (col. 11:10-18) and that the electrodes may in wide variety of forms including interdigitated arrays (col. 04:48-54). As such, the electrode arrangement would be contained in the analysis compartment. Also, Chang already has a power source for generating a dielectrophoresis field, which can generate very complicated wave forms (col. 13:19-40).

Addressing claim 62, although Chang as modified by Frenea does not specifically mention equipping the fluidic microsystem with a fluididc device for moving at least one of a suspension fluid and a treatment fluid through the analyte area, Chang does provide the fluidic microsystem with an inlet tube (41) and also an outet tube (44) to insert and remove objects from the analysis area. See Figure 4A and col. 11:23-25. Such a configuration would suggest to one with ordinary skill in the art using a pump to move fluid through the analysis area when desired.

Addressing claims 65 and 66, for the additional limitations of these claims see Figure 2 in Frenea.

8. Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fiedler et al. US 5,948,328 ("Fiedler") in view of Chang US 4,970,154 ("Chang").

Fiedler discloses a method of shaping microparticles with a high-frequency field cage in a fluidic microsystem. See the abstract and Figures 1-5. Fiedler does not mention analyzing at least one of deformation or relaxation properties of the biological cells although this is strongly suggested since Fiedler provides several figures showing analysis of the cells when subject to deformation. See, for example, Figures 1-5.

Chang disclose a method for inserting foreign genes into cells using pulsed radiofrequency. The method involves deforming biological cells by porating them or fusing them. Chang uses a power function generator that can apply a continuous AC electrical field and/or a high-power pulsed radiofrequency electrical field across the electrodes. Chang also discloses several ways of analyzing the deformation of the biological cells, such as by measuring the actual electrical field applied to the cells or optical monitoring by freeze-framed electron microscopy or fluorescent imaging. See the abstract; col. 13:35-40; col. 04:44-47; col. 17:05-20; col. 16:01-22; and col. 16:25-41. It would have been obvious to one with ordinary skill in the art at the time of the invention to provide a way to analyze at least one of deformation or relaxation properties as taught by Chang in the invention of Fiedler because this would ensure that the desired shape (deformation) has been obtained and/or allow optimization of the electrical deformation fields for subsequent deformations.

Allowable Subject Matter

9. Claims 37, 43, 50, 51, 64, and 67 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 37 – the combination of limitations requires that "... the generation of the deformation force takes place under an effect of negative dielectrophoresis or under an effect of positive dielectrophoresis."

In Chang as modified by Frenea the generation of the deformation force takes place under high-power RF pulses. See col. 03:38-40; col. 04:05-15; and col. 10:43-48.

Müller et al. US 6,492,175 B1 discloses a microsystem for cell permeation and cell fusion that uses a dielectrophoresis field to position an object. However, deformation of the object, such as cell permeation, is caused by a DC field. See the abstract; col. 02:43-65; and col. 08:54 – col. 09:10.

Fiedler et al. US 5,948,328 discloses a method of shaping microparticles in electric-field cages. However, there does not appear to be a separate generation of an electric positioning field from a generation of an electric

deformation field as claimed. Object positioning and object deformation occur simultaneously due apparently to the combined effect of different fields applied to the electrodes and the disposition and geometry of the electrodes. See the abstract; col. 02:38-56; col. 04:06-24; and col. 04:32-45.

b) Claim 43 - the combination of limitations requires that "... a separate deformation electrode arrangement is used to generate the deformation field."

In Müller the same electrode arrangement is used to generate both the positioning field and the deformation field. See col. 02:66 – col. 03:15 and col. 05:29-49.

In Chang as modified by Frenea the same electrode arrangement would be used to generate both the positioning field and the deformation field. See Chang Figure 4 and col. 10:50-54.

c) Claim 50 - the combination of limitations requires that "... at lease one of the deformation filed and the positioning field is adjusted a number of times in such a way that the object is in each case deformed in different directions."

In Chang as modified by Frenea the deformation is electroporation or electrofusion, without any apparent directional effect.

d) Claim 51 - the combination of limitations requires that "... viscoelastic properties of the object are determined from the detected dielectric, geometric or optical properties."

In Chang as modified by Frenea the permeability or extent of fusion of objects is determined. See col. 10:66 – col. 11:04 and col. 11:10-14.

In Müller the permeability or extent of fusion of objects is determined. See col. 09:49-58.

e) Claim 64 - the combination of limitations requires that "... the control device forms a control loop in which the positioning filed and/or the deformation filed can be adjusted or changed as a function of a result of the preceding detection."

In Chang as modified by Frenea the effects of a positioning field and/or the deformation field can be detected and recorded. However, such information could be used, perhaps, to optimize a subsequent analysis. There is no provision of a control loop as claimed. See Figure 14 and col. 13:19-40.

f) Claim 67 - the combination of limitations requires that "... the positioning field and the deformation field are switched on at the same time in the second operating state."

In Chang as modified by Frenea the positioning filed is switched on before and/or after the deformation field is switched on. See Chang col. 10:50-54 and col. 13:13-15.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Alex Noguerola/
Primary Examiner, Art Unit 1795
March 1, 2010